

Guidelines Regarding the Inclusion of Pregnant and Breast-Feeding Women on Cancer Clinical Treatment Trials

Pregnant women may not be arbitrarily excluded from participation in clinical cancer treatment trials. Exclusion of pregnant women from a particular trial must be based on a clear and compelling rationale or justification that shows that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research, or other circumstances that offer a clear and compelling reason for exclusion. Such rationale may include laboratory, animal or clinical evidence suggesting a treatment may be associated with potential toxicity to the fetus that exceeds the minimum risk necessary to meet the health needs of the mother or minimal risk to the fetus.

Breast-feeding women may not be arbitrarily excluded from participation in clinical cancer treatment trials. Exclusion of breast-feeding women from a particular trial must be based on a clear and compelling rationale or justification that shows that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research, or other circumstances that offer a clear and compelling reason for exclusion. Such rationale may include laboratory, animal or clinical evidence suggesting a treatment may be associated with potential toxicity to the child that exceeds the minimum risk necessary to meet the health needs of the mother or minimal risk to the child.

These guidelines are based upon the “NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research” (59 FR 14508 [March 28, 1994] at 14509), which state that women should be included in clinical trials unless

a clear and compelling rationale establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be made by the Director, NIH, upon the recommendation of an Institute/ Center Director based on a compelling rationale and justification.

Furthermore, Federal regulations at 45 C.F.R. Part 46, Subpart C, provide specific standards for including pregnant women in clinical trials. Pregnant women may be included on clinical trials only when: (1) the purpose of the trial is to meet the health needs of the mother and the fetus will be placed at risk only to the minimal extent necessary to meet such needs or (2) the risk to the fetus is minimal (45 C.F.R. 46.207[a]). Additional general limitations require that research involving pregnant women and fetuses only take place when: (1) appropriate studies on animals and nonpregnant individuals have been completed; (2) the risk to the fetus is the least possible risk for achieving the objectives of the trials, including when the purpose of the trial is to meet the health needs of the mother or the fetus, or the risk to the fetus is minimal; (3) individuals engaged in the research have no part in decisions regarding any termination of a pregnancy or viability of a fetus; (4) no procedural changes which will cause greater than minimal risk to the woman or fetus will be introduced into the procedure for terminating the pregnancy solely in the interest of the trial; and (5) no inducements are offered to terminate a pregnancy for purposes of the trial.

The Food and Drug Administration (FDA) has concluded that (1) exclusion of women from early trials is not medically necessary because the risk of fetal exposure can be minimized by patient behavior and laboratory testing, and (2) initial determinations about whether that risk is adequately addressed are properly left to patients, physicians, local IRBs and sponsors, with appropriate review and guidance by the FDA (58 FR 39406 [July 22, 1993]). The FDA stated that

appropriate precautions should be taken in clinical studies to guard against inadvertent exposure of fetuses to potentially toxic agents and to inform subjects and patients of potential risk and the need for precautions. In all cases the informed consent document and investigator's brochure should include all available information regarding the potential risk of fetal toxicity. If animal reproductive toxicity studies are complete, the results should be presented, with some explanation of their significance in humans. If these studies have not been completed, other pertinent information should be provided, such as a general assessment of fetal toxicity in drugs with related structures or pharmacologic effects. If no relevant information is available, the informed consent should explicitly note the potential for fetal risk.